Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	179	"pinanediol"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 13:30
L2	50	"pinanediol ester"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 13:30
L3	3	"pinanediol ester" and "phenylpropylboronic acid"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 13:31
L4	10	"pinanediol ester" and "phenylpropyl$"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 13:31
L5	10	"pinanediol ester" and "phenylpropyl$" and "$boronic$"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 13:32
L6	10	"pinanediol" SAME "ester" and "phenylpropyl$" and "$boronic$"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 13:32
L7	0	"pinanediol" SAME "ester" and "phenylpropyl$" and "$boronic$" and "Asp-Glu-val-val-pro"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 13:33
L8	10	"pinanediol" SAME "ester" and "phenylpropyl$" and "$boronic$" and peptide	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 13:33
L9	10	"pinanediol" SAME "ester" and "phenylpropyl$" and "$boronic$" and peptide and val and glu and pro and asp	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 13:47

L11	1	"5563127".did. and "phenylpropyl$" and peptide and val and glu and pro and asp	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 13:39
L12	10	"pinanediol" SAME "ester" and "phenylpropyl$" and "$boronic$" and val and glu and pro and asp	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 15:57
L13	34	"pinanediol" SAME "ester" and val and glu and pro and asp	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 13:48
L14	32024	val and glu and pro and asp	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 15:58
L15	27980	val SAME glu SAME pro SAME asp	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 15:59
L16	30	val SAME glu SAME pro SAME asp and pinanediol	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 15:59
L17	30	val SAME glu SAME pro SAME asp and pinanediol and acid	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 15:59
L18	30	val SAME glu SAME pro SAME asp and pinanediol and ($boron$ or $boronic$)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 16:36
L19	30	val SAME glu SAME pro SAME asp and pinanediol and ($boron$ or $boronic$) and amino	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 16:02
L20	5	514/18.ccls. and val SAME glu SAME pro SAME asp and pinanediol and ($boron$ or $boronic$)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 16:38

S1	0	"Asp-Glu-val-val-Pro"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/09 13:30
S2	0	"Asp ADJ Glu ADJ val ADJ val ADJ Pro"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/07 16:06
S3	0	"Asp SAME Glu SAME val SAME val SAME Pro"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/07 16:08
S4	0	"Asp SAME Glu SAME val SAME val SAME Pro" and 514/18.ccls.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/07 16:08
S5	3	514/18.ccls. and peptide and 5-mer	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/07 16:09
S6	2	"20040147483".did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/07 16:09
S7	0	"20040147483".did. and "Asp-Glu-val-val-Pro"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/07 16:09
S8	3	"H-Asp-Glu-val-val-Pro-"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2004/12/07 16:10

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=> d his

     FILE 'REGISTRY' ENTERED AT 08:14:37 ON 09 DEC 2004
L1           836 DEVVP/SQSP
L2           107 L1 AND B/ELS
L3           107 L2 AND NC4/ES
L4           106 C4-BOC2O-C6/ES AND L3

     FILE 'HCAPLUS' ENTERED AT 10:34:28 ON 09 DEC 2004
L5             9 L4
L6             1 (US20040147483 OR US20020177725)/PN
                 E US2000-242557/AP/PRN
                 E US2000-242557/AP,PRN
L7             1 US2000-242557P/AP,PRN
L8             1 L6-7
                 E PRIESTLEY E/AU
L9            21 E6,E9
L10        40699 (BRISTOL OR MEYER? OR MYER? OR SQUIBB)/CS,PA
L11            5 L5 AND L9-10
L12            4 L5 NOT L11

     FILE 'REGISTRY' ENTERED AT 10:44:48 ON 09 DEC 2004

     FILE 'HCAPLUS' ENTERED AT 10:44:52 ON 09 DEC 2004
L13              TRA L8 1- RN :      187 TERMS

     FILE 'REGISTRY' ENTERED AT 10:44:52 ON 09 DEC 2004
L14          187 SEA L13
L15           42 L14 AND L4

     FILE 'WPIX' ENTERED AT 10:45:21 ON 09 DEC 2004
L16            2 (US20040147483 OR US20020177725)/PN
                 E US2000-242557/AP,PRN
L17            1 US2000-242557P/AP,PRN
L18            2 L16-17

=> b hcap
FILE 'HCAPLUS' ENTERED AT 10:48:32 ON 09 DEC 2004
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FILE COVERS 1907 - 9 Dec 2004  VOL 141 ISS 24
FILE LAST UPDATED: 8 Dec 2004  (20041208/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d all l11 tot

L11  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:907216  HCAPLUS
DN   138:4821
ED   Entered STN:  29 Nov 2002
TI   Preparation of peptide inhibitors of hepatitis C virus NS3 protein
IN   Priestley, E. Scott
PA   USA
SO   U.S. Pat. Appl. Publ., 54 pp.
     CODEN: USXXCO
DT   Patent
LA   English
IC   ICM  C07F005-02
     ICS  C07F005-05; C07C237-04
NCL  558288000; 564010000; 564152000; 564502000
```

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 29, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002177725	A1	20021128	US 2001-39317	20011028
	US 2004147483	A1	20040729	US 2004-759725	20040115
PRAI	US 2000-242557P	P	20001023		
	US 2001-39317	A3	20011028		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2002177725	ICM	C07F005-02
	ICS	C07F005-05; C07C237-04
	NCL	558288000; 564010000; 564152000; 564502000

OS MARPAT 138:4821

AB The invention relates to a novel class of peptides R3-A-N(R2)CHR1-W [W = B(OH)2 or a derivative, COCO-Q, COCONH-Q, COCO2-Q, COCF2CONH-Q, COCF3, COCF2CF3, or CHO, where Q is an amino acid residue or an alkyl, alkenyl, or alkynyl radical substituted by CO2H, SO2H, SO3H, PO2H, PO3H (or their esters), etc.; A is a (di- through hepta)peptide residue; R1 = R1a(CH2)2-6 (R1a = substituted phenyl), BuCH2, BuCH2CH2, Me3C(CH2)3, Et2CH(CH2)3, or 3-cyclobutylpropyl; R2 = H, alkyl, aryl, arylalkyl, or cycloalkyl; R3 = H, alkyl, aryl, arylalkyl, COR11, CO2R11, CONHR11, SOR11, SO2R11 (R11 = alkyl, aryl, or heterocyclyl which may be substituted), or an NH2-blocking group] which are useful as serine protease inhibitors, more particularly as hepatitis C virus (HCV) NS3 protease inhibitors. Thus, H-Asp-Glu-Val-Val-Pro-(R)-amino(phenyl)methylboronic acid (+)-pinanediol ester was prepared by solution phase chemical Compds. of the invention were found to exhibit a Ki of ≤ 50 μM, thereby confirming their utility as effective HCV NS3 protease inhibitors.

ST peptide boronate prepn hepatitis C virus NS3 protease inhibitor

IT Hepatitis
(C; preparation of peptide inhibitors of hepatitis C virus NS3 protein)

IT Antiviral agents
(preparation of peptide inhibitors of hepatitis C virus NS3 protein)

IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide inhibitors of hepatitis C virus NS3 protein)

IT 149885-80-3, Ns3 protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of peptide inhibitors of hepatitis C virus NS3 protein)

IT 274918-51-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of peptide inhibitors of hepatitis C virus NS3 protein)

IT **476333-92-3P 476333-93-4P 476333-94-5P**
476333-95-6P 476333-96-7P 476333-97-8P
476333-98-9P 476333-99-0P 476334-00-6P
476334-01-7P 476334-02-8P 476334-03-9P
476334-04-0P 476334-05-1P 476334-06-2P
476334-07-3P 476334-08-4P 476334-10-8P
476334-11-9P 476334-12-0P 476334-13-1P
476334-14-2P 476334-15-3P 476334-16-4P
476334-17-5P 476334-18-6P 476334-19-7P 476334-20-0P
476334-21-1P 476334-22-2P 476334-23-3P 476334-24-4P
476334-25-5P 476334-26-6P 476334-27-7P
476334-28-8P 476334-29-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide inhibitors of hepatitis C virus NS3 protein)

IT 98-80-6, Phenylboric acid 100-80-1, 3-Methylstyrene 274-07-7, Catecholborane 350-51-6, 3-Fluorostyrene 394-46-7, 2-Fluorostyrene 402-24-4, 3-Trifluoromethylstyrene 402-50-6, 4-Trifluoromethylstyrene 405-99-2, 4-Fluorostyrene 611-15-4, 2-Methylstyrene 622-97-9, 4-Methylstyrene 637-59-2, 1-Bromo-3-phenylpropane 637-69-4, 4-Methoxystyrene 693-25-4, Pentylmagnesium bromide 1073-67-2, 4-Chlorostyrene 1746-23-2, 4-tert-Butylstyrene 2039-82-9, 4-Bromostyrene 2039-89-6, 2,5-Dimethylstyrene 2055-40-5, 4-Isopropylstyrene 2234-20-0, 2,4-Dimethylstyrene 2350-89-2, 4-Vinylbiphenyl 3761-92-0, Hexylmagnesium bromide 4399-47-7, Cyclobutyl bromide 4830-93-7, 1-Chloro-4-phenylbutane 4973-29-9,

4-Phenoxystyrene 5419-55-6, Triisopropyl borate 5720-05-8,
4-Methylphenylboronic acid 5720-07-0, 4-Methoxyphenylboronic acid
13020-34-3, 4-Cyclohexylstyrene 13686-49-2, 1-(2-Bromoethyl)naphthalene
18680-27-8 37586-57-5, 4-Methyl-3-pentenylmagnesium bromide
90878-19-6, Phenethyl magnesium chloride 95418-58-9, 4-t-Butoxystyrene
207226-37-7, 2,6-Difluorostyrene
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptide inhibitors of hepatitis C virus NS3 protein)

IT 14650-23-8P 16746-85-3P 50715-50-9P 58872-03-0P 76110-78-6P
76110-79-7P 99429-45-5P 99429-46-6P 106665-76-3P 130292-03-4P
192193-55-8P 244782-33-0P 244782-34-1P 289709-75-7P 319011-74-0P
319011-76-2P 319012-18-5P 476334-31-3P **476334-32-4P**
476334-33-5P **476334-34-6P** 476334-35-7P 476334-36-8P
476334-37-9P **476334-38-0P** 476334-39-1P 476334-40-4P
476334-41-5P **476334-42-6P** 476334-43-7P 476334-44-8P
476334-45-9P **476334-46-0P** 476334-47-1P 476334-48-2P
476334-49-3P 476334-50-6P 476334-51-7P 476334-52-8P 476334-53-9P
476334-54-0P 476334-55-1P 476334-56-2P 476334-57-3P 476334-58-4P
476334-59-5P 476334-60-8P 476334-61-9P 476334-62-0P 476334-63-1P
476334-64-2P 476334-65-3P 476334-66-4P 476334-67-5P 476334-68-6P
476334-69-7P 476334-70-0P 476334-71-1P 476334-72-2P 476334-73-3P
476334-74-4P 476334-75-5P 476334-76-6P **476334-77-7P**
476334-78-8P 476334-79-9P 476334-80-2P 476334-81-3P 476334-82-4P
476334-83-5P 476334-84-6P 476334-85-7P 476334-86-8P 476334-87-9P
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476334-94-8P 476334-95-9P 476334-96-0P 476334-97-1P 476334-98-2P
476334-99-3P 476335-00-9P 476335-01-0P 476335-02-1P 476335-03-2P
476335-04-3P 476335-05-4P 476335-06-5P 476335-07-6P 476335-08-7P
476335-09-8P 476335-10-1P 476335-11-2P **476335-12-3P**
476335-13-4P 476335-14-5P 476335-15-6P **476335-16-7P**
476335-17-8P 476335-18-9P 476335-19-0P **476335-20-3P**
476335-21-4P 476335-22-5P 476335-23-6P **476335-24-7P**
476335-25-8P 476335-26-9P 476335-27-0P **476335-28-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide inhibitors of hepatitis C virus NS3 protein)

L11 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:767330 HCAPLUS
DN 138:221813
ED Entered STN: 09 Oct 2002
TI P1 Phenethyl peptide boronic acid inhibitors of HCV NS3 protease
AU **Priestley, E. Scott**; De Lucca, Indawati; Ghavimi, Bahman; Erickson-Viitanen, Susan; Decicco, Carl P.
CS Experimental Station, **Bristol-Myers Squibb** Pharmaceutical Research Institute, Wilmington, DE, 19880-0500, USA
SO Bioorganic & Medicinal Chemistry Letters (2002), 12(21), 3199-3202
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 15, 29
AB A series of peptide boronic acids containing extended, hydrophobic P1 residues was prepared to probe the shallow, hydrophobic S1 region of HCV NS3 protease. The p-trifluoromethylphenethyl P1 substituent was identified as optimal with respect to inhibitor potency for NS3 and selectivity against elastase and chymotrypsin.
ST P1 phenethyl peptide boronic acid inhibitor protease; hepatitis C virus NS3 protease inhibitor boronic peptide prepn; structure activity boronic peptide protease inhibitor
IT Structure-activity relationship
(enzyme-inhibiting; preparation of P1 phenethyl peptide boronic acid inhibitors of HCV NS3 protease)
IT Hepatitis C virus
(preparation of P1 phenethyl peptide boronic acid inhibitors of HCV NS3 protease)
IT 9004-06-2, Elastase 9004-07-3, Chymotrypsin 149885-80-3, Ns3 protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of P1 phenethyl peptide boronic acid inhibitors of HCV NS3 protease)
IT **500763-17-7P 500763-19-9P 500763-21-3P**
500763-23-5P 500763-25-7P 500763-27-9P
500763-29-1P 500763-31-5P 500763-33-7P
500763-35-9P 500763-37-1P 500763-39-3P
500763-42-8P 500763-44-0P 500763-46-2P

500763-48-4P 500763-50-8P 500763-52-0P
500763-53-1P 500763-55-3P 500763-57-5P
500763-59-7P 500763-61-1P 500763-63-3P
500763-65-5P 500763-67-7P 500763-69-9P
500763-71-3P 500763-73-5P 500763-74-6P
500763-75-7P 500763-76-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of P1 phenethyl peptide boronic acid inhibitors of HCV NS3 protease)

IT 98-80-6, Phenylboronic acid 100-58-3, Phenylmagnesium bromide 100-80-1, 3 Methylstyrene 350-51-6, 3 Fluorostyrene 394-46-7, 2 Fluorostyrene 402-24-4, 3 Trifluoromethylstyrene 402-50-6, 4 Trifluoromethylstyrene 405-99-2, 4 Fluorostyrene 611-15-4, 2 Methylstyrene 622-97-9, 4 Methylstyrene 637-69-4, 4 Methoxystyrene 693-03-8, Butylmagnesium bromide 693-25-4, Pentylmagnesium bromide 925-90-6, Ethylmagnesium bromide 926-62-5, Isobutylmagnesium bromide 1073-67-2, 4 Chlorostyrene 1462-75-5 1589-82-8, Benzylmagnesium bromide 1746-23-2, 4 tert Butylstyrene 2039-82-9, 4 Bromostyrene 2039-89-6, 2 5 Dimethylstyrene 2055-40-5, 4 Isopropylstyrene 2146-67-0, Dichloromethyllithium 2234-20-0, 2 4 Dimethylstyrene 2350-89-2, 4 Phenylstyrene 2628-17-3, 4 Hydroxystyrene 3277-89-2, Phenethylmagnesium bromide 3761-92-0, Hexylmagnesium bromide 4548-78-1, Isopentylmagnesium bromide 4973-29-9, 4 Phenoxystyrene 5419-55-6, Triisopropyl borate 7429-94-9, 4-Methylpentylmagnesium bromide 13020-34-3, 4 Cyclohexylstyrene 18680-27-8 27152-04-1 207226-37-7, 2 6 Difluorostyrene 274918-51-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of P1 phenethyl peptide boronic acid inhibitors of HCV NS3 protease)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Bartenschlager, R; J Gen Virol 2000, V81, P1631 HCAPLUS
(2) Bartenschlager, R; J Viral Hepatitis 1999, V6, P165 MEDLINE
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L11 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:466017 HCAPLUS
DN 137:47198
ED Entered STN: 21 Jun 2002
TI Imidazolidinones and their related derivatives as Hepatitis C virus NS3 protease inhibitors
IN Han, Qi
PA **Bristol-Myers Squibb** Pharma Company, USA
SO PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07F005-02
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 29, 34

FAN.CNT 1

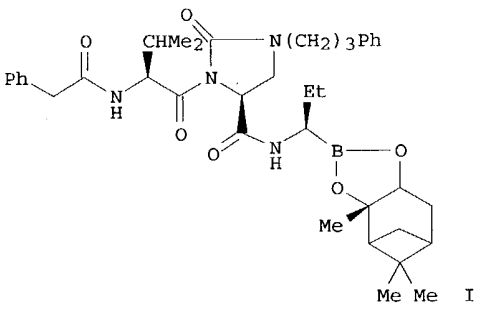
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2002048157 A2 20020620 WO 2001-US47916 20011212
WO 2002048157 A3 20030327
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2002030764 A5 20020624 AU 2002-30764 20011212
US 2003100768 A1 20030529 US 2001-15328 20011212
US 6727366 B2 20040427
PRAI US 2000-255168P P 20001213
WO 2001-US47916 W 20011212

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002048157	ICM	C07F005-02
US 2003100768	ECLA	C07D233/32; C07D233/38; C07F005/02C; C07K005/06T; C07K007/06A

OS MARPAT 137:47198
GI



I

AB Title compds. were prepared for use as serine protease inhibitors, especially Hepatitis C virus NS3 protease inhibitors (no data). Thus, the imidazolidinone I was obtained from (S)-(-)-N-benzyloxycarbonyl-2-oxo-5-imidazolidinecarboxylic acid and the dioxaborolane fragment in 8 steps.

ST benzodioxaborolylpropyl imidazolidinecarboxamide prepn hepatitis virus protease inhibitor

IT Hepatitis C virus
(preparation of N-(benzodioxaborolylpropyl)imidazolidinecarboxamides as hepatitis C virus NS3 protease inhibitors)

IT 149885-80-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hepatitis C virus; preparation of N-(benzodioxaborolylpropyl)imidazolidinecarboxamides as hepatitis C virus NS3 protease inhibitors)

IT **319010-09-8P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of N-(benzodioxaborolylpropyl)imidazolidinecarboxamides as hepatitis C virus NS3 protease inhibitors)

IT 103-80-0, Phenylacetyl chloride 454-89-7, 3-Trifluoromethylbenzaldehyde 1676-90-0 5292-43-3, tert.-Butyl bromoacetate 13734-41-3, N-tert.-Butoxycarbonyl-L-valine 26146-77-0, (E)-Cinnamyl bromide 41324-66-7, L-Proline benzyl ester 59760-01-9 103321-53-5 212001-41-7, 4-Bromomethyl-2-phenylquinoline 319009-92-2 323197-73-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-(benzodioxaborolylpropyl)imidazolidinecarboxamides as hepatitis C virus NS3 protease inhibitors)

IT 50715-50-9P 58872-03-0P 99429-45-5P 106665-76-3P 168399-08-4P 274918-51-3P **319010-06-5P** 319011-72-8P 319011-74-0P 319011-76-2P 437755-63-0P 437755-64-1P 437755-65-2P 437755-66-3P 437755-68-5P 437755-69-6P 437755-70-9P 437755-71-0P 437755-72-1P 437755-73-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of N-(benzodioxaborolylpropyl)imidazolidinecarboxamides as hepatitis C virus NS3 protease inhibitors)

IT 437755-43-6P 437755-44-7P 437755-45-8P 437755-46-9P 437755-47-0P
437755-48-1P 437755-49-2P 437755-50-5P 437755-51-6P 437755-52-7P
437755-53-8P 437755-54-9P 437755-55-0P 437755-56-1P 437755-57-2P
437755-58-3P 437755-59-4P 437755-60-7P 437755-61-8P 437755-62-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-(benzodioxaborolylpropyl)imidazolidinecarboxamides as hepatitis C virus NS3 protease inhibitors)

L11 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:465982 HCAPLUS
DN 137:47213
ED Entered STN: 21 Jun 2002
TI Preparation of fused pyrimidinones and benzodioxaborolidinylpropylaminopyrrolo[1,2-a]pyrimidines as inhibitors of hepatitis C ns3 protease for the treatment of hepatitis C and other viral diseases
IN Glunz, Peter W.; Douty, Brent D.; Han, Wei
PA **Bristol-Myers Squibb** Pharma Company, USA
SO PCT Int. Appl., 270 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D239-00
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002048116	A2	20020620	WO 2001-US47911	20011212
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002030763	A5	20020624	AU 2002-30763	20011212
	US 2003064962	A1	20030403	US 2001-15304	20011212
	US 6653295	B2	20031125		
PRAI	US 2000-255290P	P	20001213		
	WO 2001-US47911	W	20011212		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002048116	ICM	C07D239-00
US 2003064962	ECLA	A61K047/48R2; C07D471/04+239C+221C; C07D487/04+239C+209C; C07F005/02C; C07F005/04; C07K005/06H4;

OS MARPAT 137:47213
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Fused pyrimidinones I [A1 = (un)substituted CH2, CH2CH2, CH2CH2CH2, A2CH2, A2CH2CH2, CH2A2CH2; A2 = O, S, (un)substituted imino; A3 = H, R9CO, R9O, R9S, R9CONH, R9NHCO, etc.; W = (un)substituted boronic acid ester, QCOCO, QNHCOCO, QOCOCO, QNHCOCF2CO, COQ3, F3CCO, F3CCF2CO, OHC, amino acid residue; Q3 = (un)substituted aryl, heterocyclyl; R1 = H, F, (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl; R2 = H, alkyl; Q, R3, R9 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl; R6, R13 = H, (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, cycloalkylalkyl; R3R13 = (un)substituted carbocyclic ring, alkylidene] and particularly dioxaborolylpropylamino pyrrolopyriminecarboxamides such as II are prepared as inhibitors of hepatitis C viral protein ns3 protease for the treatment of hepatitis C and other viral diseases. E.g., esterification of L-pyroglutamic acid with AcOCMe3 and HClO4, thionation with Lawesson's reagent, S-methylation with MeI, and amidation with NH4Cl gives nonracemic

aminopyrrolinecarboxylate III. Treatment of III with di-Me 2-(methoxymethylene)malonate, hydrolysis of the Me ester moiety with LiOH, preparation of the acyl azide with diphenylphosphoryl azide and Curtius rearrangement in the presence of PhCH2OH, and hydrolysis of the tert-Bu ester with CF3CO2H gives pyrrolo[1,2-a]pyrimidine IV. Coupling of IV with an α-allyl aminomethylboronate pinanediol ester gives II. I inhibit hepatitis C ns3 protease with IC50 values of <100 μM. Pharmaceutical compns. containing I are given.

ST fused pyrimidinone prepn hepatitis C NS3 inhibitor; benzodioxaborolidinylpropylamino pyrrolopyrimidine prepn hepatitis C NS3 inhibitor; benzodioxaborolidinylpropylaminopyrrolopyrimidine prepn hepatitis C NS3 inhibitor; benzodioxaborolidinyl propylamino pyrrolopyrimidine prepn hepatitis C NS3 inhibitor; antiviral fused pyrimidinone prepn

IT Hepatitis
(C, infection treatment; preparation of fused pyrimidinones and benzodioxaborolidinylpropylaminopyrrolo[1,2-a]pyrimidines as inhibitors of hepatitis C ns3 protease for the treatment of hepatitis C and other viral diseases)

IT Antiviral agents
Hepatitis C virus
(preparation of fused pyrimidinones and benzodioxaborolidinylpropylaminopyrrolo[1,2-a]pyrimidines as inhibitors of hepatitis C ns3 protease for the treatment of hepatitis C and other viral diseases)

IT 204765-53-7 438493-20-0
RL: PRP (Properties)
(Unclaimed; preparation of fused pyrimidinones and benzodioxaborolidinylpropylaminopyrrolo[1,2-a]pyrimidines as inhibitors of hepatitis C ns3 protease for the treatment of hepatitis C and other viral diseases)

IT 149885-80-3, NS3 protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hepatitis C, inhibitors; preparation of fused pyrimidinones and benzodioxaborolidinylpropylaminopyrrolo[1,2-a]pyrimidines as inhibitors of hepatitis C ns3 protease for the treatment of hepatitis C and other viral diseases)

IT 35418-16-7P 81470-51-1P 102056-99-5P 227616-72-0P 227616-73-1P
227616-74-2P 227616-75-3P 227616-76-4P 227616-77-5P 437754-05-7P
437760-93-5P 437760-94-6P 437760-95-7P 437760-96-8P 437760-97-9P
437760-98-0P 437760-99-1P 437761-00-7P 437761-01-8P 437761-02-9P
437761-03-0P 437761-04-1P 437761-05-2P 437761-06-3P 437761-07-4P
437761-08-5P 437761-09-6P 437761-10-9P 437761-11-0P 437761-12-1P
437761-13-2P 437761-14-3P 437761-15-4P 437761-16-5P 437761-17-6P
437761-18-7P 437761-19-8P 437761-20-1P 437761-21-2P 437761-22-3P
437761-23-4P 437761-24-5P 437761-25-6P 437761-26-7P 437761-27-8P
437761-28-9P 437761-29-0P 437761-30-3P 437761-32-5P 437761-33-6P
437761-34-7P 437761-35-8P 437761-36-9P 437761-37-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of fused pyrimidinones and benzodioxaborolidinylpropylaminopyrrolo[1,2-a]pyrimidines as inhibitors of hepatitis C ns3 protease for the treatment of hepatitis C and other viral diseases)

IT 437758-27-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(invention compound; preparation of fused pyrimidinones and benzodioxaborolidinylpropylaminopyrrolo[1,2-a]pyrimidines as inhibitors of hepatitis C ns3 protease for the treatment of hepatitis C and other viral diseases)

IT 437758-26-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(invention compound; preparation of fused pyrimidinones and benzodioxaborolidinylpropylaminopyrrolo[1,2-a]pyrimidines as inhibitors of hepatitis C ns3 protease for the treatment of hepatitis C and other viral diseases)

IT 437758-28-6P 437758-33-3P 437758-34-4P 437759-44-9P 437759-95-0P
437760-35-5P 437760-37-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(invention compd; preparation of fused pyrimidinones and benzodioxaborolidinylpropylaminopyrrolo[1,2-a]pyrimidines as inhibitors

of hepatitis C ns3 protease for the treatment of hepatitis C and other viral diseases)

IT 437758-29-7P 437758-30-0P 437758-31-1P 437758-32-2P 437758-35-5P
437758-36-6P 437758-38-8P 437758-39-9P 437758-40-2P 437758-41-3P
437758-42-4P 437758-43-5P 437758-44-6P 437758-45-7P 437758-46-8P
437758-47-9P 437758-48-0P 437758-49-1P 437758-50-4P 437758-51-5P
437758-52-6P 437758-53-7P 437758-54-8P 437758-55-9P 437758-56-0P
437758-57-1P 437758-58-2P 437758-59-3P 437758-60-6P 437758-61-7P
437758-62-8P 437758-63-9P 437758-64-0P 437758-65-1P 437758-66-2P
437758-67-3P 437758-68-4P 437758-69-5P 437758-70-8P 437758-71-9P
437758-72-0P 437758-73-1P 437758-74-2P 437758-75-3P 437758-76-4P
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437759-89-2P 437759-90-5P 437759-91-6P 437759-92-7P 437759-93-8P
437759-94-9P 437759-96-1P 437759-97-2P 437759-98-3P 437759-99-4P
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437760-10-6P 437760-11-7P 437760-12-8P 437760-13-9P 437760-14-0P
437760-15-1P 437760-16-2P 437760-17-3P 437760-18-4P 437760-19-5P
437760-20-8P 437760-21-9P 437760-22-0P 437760-23-1P 437760-24-2P
437760-25-3P 437760-27-5P 437760-28-6P 437760-29-7P 437760-30-0P
437760-31-1P 437760-32-2P 437760-33-3P 437760-38-8P 437760-39-9P
437760-40-2P 437760-41-3P 437760-42-4P 437760-43-5P 437760-44-6P
437760-45-7P 437760-46-8P 437760-47-9P 437760-48-0P 437760-49-1P
437760-50-4P 437760-51-5P 437760-52-6P 437760-53-7P 437760-54-8P
437760-55-9P 437760-56-0P 437760-57-1P 437760-58-2P 437760-59-3P
437760-60-6P 437760-61-7P 437760-62-8P 437760-63-9P 437760-64-0P
437760-65-1P 437760-66-2P 437760-67-3P 437760-68-4P 437760-69-5P
437760-70-8P 437760-71-9P 437760-72-0P 437760-73-1P 437760-74-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(invention compd; preparation of fused pyrimidinones and benzodioxaborolidinylpropylaminopyrrolo[1,2-a]pyrimidines as inhibitors of hepatitis C ns3 protease for the treatment of hepatitis C and other viral diseases)

IT 437760-75-3P 437760-76-4P 437760-77-5P 437760-78-6P 437760-79-7P
437760-80-0P 437760-81-1P 437760-82-2P 437760-83-3P 437760-84-4P
437760-85-5P 437760-86-6P 437760-87-7P 437760-88-8P 437760-91-3P
437760-92-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(invention compd; preparation of fused pyrimidinones and benzodioxaborolidinylpropylaminopyrrolo[1,2-a]pyrimidines as inhibitors of hepatitis C ns3 protease for the treatment of hepatitis C and other viral diseases)

IT **319010-09-8P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of an assay substrate inhibitor for hepatitis C ns3 protease in the testing of fused pyrimidinone and benzodioxaborolidinylpropylaminop yrrolo[1,2-a]pyrimidine inhibitors of hepatitis C ns3 protease)

IT 1676-90-0 6066-82-6, N-Hydroxysuccinimide 13734-41-3 41324-66-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of an assay substrate inhibitor for hepatitis C ns3 protease in

the testing of fused pyrimidinone and benzodioxaborolidinylpropylaminop
yrrolo[1,2-a]pyrimidine inhibitors of hepatitis C ns3 protease)

IT 58872-03-0P 99429-45-5P 106665-76-3P 274918-51-3P
319010-06-5P 319011-72-8P 319011-74-0P 319011-76-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of an assay substrate inhibitor for hepatitis C ns3 protease in the testing of fused pyrimidinone and benzodioxaborolidinylpropylaminop
yrrolo[1,2-a]pyrimidine inhibitors of hepatitis C ns3 protease)

IT 86-84-0, 1-Naphthyl isocyanate 88-68-6, 2-Aminobenzamide 90-04-0, o-Anisidine 91-21-4, 1,2,3,4-Tetrahydroisoquinoline 92-54-6, 1-Phenylpiperazine 92-67-1, 4-Aminobiphenyl 98-16-8, 3-(Trifluoromethyl)aniline 98-79-3, L-Pyroglutamic acid 99-98-9, N,N-Dimethyl-1,4-phenylenediamine 100-52-7, Benzaldehyde, reactions 102-36-3, 3,4-Dichlorophenyl isocyanate 103-71-9, Phenyl isocyanate, reactions 103-80-0, Phenylacetyl chloride 104-12-1, 4-Chlorophenyl isocyanate 132-60-5, 2-Phenyl-4-quinolinecarboxylic acid 134-32-7, 1-Aminonaphthalene 329-01-1, 3-(Trifluoromethyl)phenyl isocyanate 404-71-7, 3-Fluorophenyl isocyanate 454-89-7, 3-(Trifluoromethyl)benzaldehyde 462-08-8, 3-Aminopyridine 504-29-0, 2-Aminopyridine 536-90-3, m-Anisidine 580-22-3, 2-Aminoquinoline 611-34-7, 5-Aminoquinoline 614-68-6, o-Tolyl isocyanate 619-45-4, Methyl 4-aminobenzoate 622-58-2, p-Tolyl isocyanate 623-04-1, 4-Aminobenzyl alcohol 700-87-8, 2-Methoxyphenyl isocyanate 769-92-6, 4-tert-Butylaniline 1016-19-9, 3,4,5-Trimethoxyphenyl isocyanate 1195-45-5, 4-Fluorophenyl isocyanate 1532-84-9, 1-Aminoisoquinoline 1548-13-6, 4-(Trifluoromethyl)phenyl isocyanate 1632-84-4, 4-(Methylthio)phenyl isocyanate 1783-81-9, 3-(Methylthio)aniline 1793-07-3, Methyl 2-isocyanatobenzoate 1795-48-8, Isopropyl isocyanate 1885-14-9, Phenyl chloroformate 1943-67-5, 4-tert-Butylphenyl isocyanate 1943-82-4, Phenethyl isocyanate 2243-54-1, 2-Naphthyl isocyanate 2285-12-3, 2-(Trifluoromethyl)phenyl isocyanate 2759-28-6, 1-Benzylpiperazine 3173-56-6, Benzyl isocyanate 3320-83-0, 2-Chlorophenyl isocyanate 3320-86-3, 2-Nitrophenyl isocyanate 4141-08-6, N-Methyl-2-aminobenzamide 4461-33-0, Benzoyl isocyanate 4461-36-3, p-Chlorobenzoyl isocyanate 5292-43-3, tert-Butyl bromoacetate 5344-90-1, 2-Aminobenzyl alcohol 5395-71-1, 2-Ethoxyphenyl isocyanate 5416-93-3, 4-Methoxyphenyl isocyanate 5855-52-7, 2-Phenylquinolin-4-amine 6526-66-5, N,N-Dimethyl-2-aminobenzamide 6628-04-2, 4-Amino-2-methylquinoline 14649-03-7, (S)-1-Phenylethyl isocyanate 16315-59-6, 4-(Dimethylamino)phenyl isocyanate 16413-26-6, 3-Cyanophenyl isocyanate 16744-98-2, 2-Fluorophenyl isocyanate 17337-13-2, 2-Biphenyl isocyanate 18680-27-8 18908-07-1, 3-Methoxyphenyl isocyanate 19735-13-8, 3-Methyl-3-phenylpiperidine 20662-53-7 22398-14-7, Dimethyl methoxymethylenemalonate 23138-50-3, 4-Ethylphenyl isocyanate 23138-64-9, 3-Acetylphenyl isocyanate 26146-77-0, trans-Cinnamyl bromide 28178-42-9, 2,6-Diisopropylphenyl isocyanate 28479-19-8, 3-(Methylthio)phenyl isocyanate 30293-86-8 30806-83-8, Ethyl 4-isocyanatobenzoate 31027-31-3, 4-Isopropylphenyl isocyanate 31166-44-6, Benzyl 1-piperazinecarboxylate 31252-42-3, 4-Benzylpiperidine 32459-62-4, 4-Ethoxyphenyl isocyanate 33375-06-3 35019-96-6, trans-2-Phenylcyclopropyl isocyanate 35037-73-1, 4-(Trifluoromethoxy)phenyl isocyanate 39718-32-6, 2,5-Difluorophenyl isocyanate 41221-47-0, Methyl 3-isocyanatobenzoate 42340-98-7 46828-05-1, Dimethyl 5-isocyanatoisophthalate 49647-20-3, 4-Acetylphenyl isocyanate 51135-96-7, 4-Benzyl-4-hydroxypiperidine 51310-19-1, Butyl 2-isocyanatobenzoate 51388-20-6, 4-Benzyloxyaniline hydrochloride 51639-48-6 52260-30-7, 2-(Methylthio)phenyl isocyanate 55225-88-2, 3-(Trifluoromethylthio)phenyl isocyanate 55440-54-5, 5-Chloro-2-methoxyphenyl isocyanate 55440-55-6, 5-Chloro-2,4-dimethoxyphenyl isocyanate 56309-56-9, 2-Isopropylphenyl isocyanate 56309-62-7, 2,5-Dimethoxyphenyl isocyanate 59025-55-7, 2,4-Difluorophenyl isocyanate 59377-19-4, 4-Phenoxyphenyl isocyanate 59377-20-7, 2-Phenoxyphenyl isocyanate 65079-19-8, 6-Amino-2-methylquinoline 65295-69-4, 2,6-Difluorophenyl isocyanate 67531-68-4, Ethyl 3-isocyanatobenzoate 76393-16-3, Ethyl 2-isocyanatobenzoate 84370-87-6, 2,4-Dimethoxyphenyl isocyanate 190774-51-7, 4-Fluoro-2-nitrophenyl isocyanate 208521-42-0 323197-73-5 359028-93-6 437761-38-1, tert-Butyl 2-isocyanatobenzoate
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of fused pyrimidinones and benzodioxaborolidinylpropylaminopyrrolo[1,2-a]pyrimidines as inhibitors of hepatitis C ns3 protease for the treatment of hepatitis C and other viral diseases)

IT 438493-18-6 438493-19-7 438525-66-7
RL: PRP (Properties)

(unclaimed sequence; preparation of fused pyrimidinones and benzodioxaborolidinylpropylaminopyrrolo[1,2-a]pyrimidines as inhibitors of hepatitis C ns3 protease for the treatment of hepatitis C and other viral diseases)

L11 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:607748 HCAPLUS
DN 133:335259
ED Entered STN: 01 Sep 2000
TI 1-Aminocyclopropaneboronic Acid: Synthesis and Incorporation into an Inhibitor of Hepatitis C Virus NS3 Protease
AU **Priestley, E. Scott**; Decicco, Carl P.
CS Department of Chemical and Physical Sciences, DuPont Pharmaceuticals Company, Wilmington, DE, 19880, USA
SO Organic Letters (2000), 2(20), 3095-3097
CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal
LA English
CC 29-4 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 7, 34
OS CASREACT 133:335259
AB The previously unreported α,α-disubstituted 1-aminoboronate esters have potential utility in peptidomimetic design, particularly against serine protease targets. A concise synthesis of 1-aminocyclopropaneboronate pinanediol ester is reported, and a peptidyl derivative has modest affinity (Ki = 1.6 μM) for hepatitis C NS3 protease. Analogs with iso-Pr and cyclohexyl in place of cyclopropyl were also prepared and tested.
ST aminocyclopropaneboronate pinanediol ester peptidyl deriv prepn NS3 protease inhibition; boronate aminocyclopropane peptidyl deriv prepn NS3 protease inhibition; explosion hazard cyclopropyl isocyanide reaction
IT Safety
(explosion hazard in reaction of cyclopropyl isocyanide during synthesis of 1-aminocyclopropaneboronic acid derivs.)
IT Explosion
(in reaction of cyclopropyl isocyanide during synthesis of 1-aminocyclopropaneboronic acid derivs.)
IT Hepatitis C virus
(synthesis of 1-aminocyclopropaneboronic acid and incorporation into inhibitor of NS3 protease of)
IT Peptidomimetics
(synthesis of 1-aminocyclopropaneboronic acid having utility in peptidomimetic design)
IT 274918-51-3, Boc-Asp(O-t-Bu)-Glu(O-t-Bu)-Val-Val-Pro-OH
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling with α,α-disubstituted 1-aminoboronate esters)
IT 58644-54-5, N-Cyclopropylformamide
RL: RCT (Reactant); RACT (Reactant or reagent)
(dehydration with tosyl chloride and tributylamine)
IT 58644-53-4P, Cyclopropyl isocyanide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(explosion hazard during reaction; preparation and lithiation followed by metathesis with triisopropyl borate in preparation of α,α-disubstituted 1-aminoboronate ester)
IT 5419-55-6, Triisopropyl borate 18680-27-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(for preparation of α,α-disubstituted 1-aminoboronate esters)
IT 149885-80-3, NS3 Protease
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(hepatitis C virus; synthesis of α,α-disubstituted 1-aminoboronate esters and incorporation into inhibitor of)
IT 598-45-8, Isopropyl isocyanide 931-53-3, Cyclohexyl isocyanide
RL: RCT (Reactant); RACT (Reactant or reagent)
(lithiation followed by metathesis with triisopropyl borate in preparation of α,α-disubstituted 1-aminoboronate ester)
IT **303191-80-2P 303191-81-3P 303191-82-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and activity as inhibitor of hepatitis C NS3 protease)
IT 303191-71-1P 303191-72-2P 303191-73-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and conversion to amine hydrochloride using methanolic hydrogen chloride)
IT 303191-74-4P 303191-75-5P 303191-76-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and coupling with pentapeptide)
IT **303191-77-7P 303191-78-8P 303191-79-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of)
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Cohen, J; Science (Washington, D C) 1999, V285, P26 HCAPLUS
(2) Davis, G; N Engl J Med 1998, V339, P1493 HCAPLUS
(3) de Francesco, R; Antiviral Ther 1998, V3(Supplement 3), P99
(4) Graciani, N; unpublished data
(5) Hoppe, D; Angew Chem, Int Ed Engl 1974, V13, P789
(6) Jagannathan, S; unpublished data
(7) Kettner, C; J Biol Chem 1984, V259, P15106 HCAPLUS
(8) Liang, T; Ann Intern Med 2000, V132, P296 HCAPLUS
(9) Llinas-Brunet, M; WO 9907733 HCAPLUS
(10) Matsumoto, K; J Org Chem 1973, V38, P2094 HCAPLUS
(11) Matteson, D; Organometallics 1984, V3, P1284 HCAPLUS
(12) Matteson, D; Organometallics 1984, V3, P614 HCAPLUS
(13) McHutchison, J; N Engl J Med 1998, V339, P1485 HCAPLUS
(14) Poynard, T; Lancet 1998, V352, P1426 HCAPLUS
(15) Redshaw, S; Emerging Drugs 1997, V2, P127 HCAPLUS
(16) Schechter, I; Biochem Biophys Res Commun 1967, V27, P157 HCAPLUS
(17) Schollkopf, U; Angew Chem, Int Ed Engl 1968, V7, P805
(18) Schollkopf, U; Liebigs Ann Chem 1976, P183
(19) Taliani, M; Anal Biochem 1996, V240, P60 HCAPLUS
(20) Urbani, A; J Biol Chem 1997, V272, P9204 HCAPLUS
(21) Versleijen, J; Tetrahedron Lett 1995, V36, P2109 HCAPLUS
(22) Zhang, R; J Virol 1997, V71, P6208 HCAPLUS

=> d all l12 tot

L12 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:923982 HCAPLUS
DN 136:50277
ED Entered STN: 21 Dec 2001
TI Hepatitis C protease NS3 exosite for inhibitor design
IN Kettner, Charles A.; Hixon, Mark S.
PA Dupont Pharmaceuticals Company, USA
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N009-00
CC 7-3 (Enzymes)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001096540	A2	20011220	WO 2001-US18751	20010608
WO 2001096540	A3	20030306		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002102533	A1	20020801	US 2001-878579	20010611
PRAI US 2000-210900P	P	20000611		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001096540	ICM	C12N009-00

AB This invention relates to a novel method of hepatitis C protease inhibition through interaction with a novel exosite remote from the active site but overlapping with P4'-P6' region of the extended substrate binding site. In particular, the present invention provides a description of a

region of the enzyme and structure activity relationships of peptides with affinity for this exosite. Ligands binding in the exosite are competitive with larger substrates such as the physiol. substrate. As such, exploitation of the exosite represents a therapeutic for the hepatitis C disease.

ST hepatitis C virus protease NS3 exosite inhibitor design

IT Hepatitis
(C, antivirals for; hepatitis C protease NS3 exosite for inhibitor design)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NS4A (nonstructural, 4A); hepatitis C protease NS3 exosite for inhibitor design)

IT Enzyme functional sites
(exosite overlapping with P4'-P6' region of the extended substrate binding site; hepatitis C protease NS3 exosite for inhibitor design)

IT Drug design
Drug screening
Hepatitis C virus
(hepatitis C protease NS3 exosite for inhibitor design)

IT Antiviral agents
(hepatitis C-specific; hepatitis C protease NS3 exosite for inhibitor design)

IT Enzyme kinetics
(of inhibition; hepatitis C protease NS3 exosite for inhibitor design)

IT 182253-67-4 208939-95-1 208939-96-2 208939-97-3 208940-11-8
241823-21-2 381209-64-9 381209-65-0 381209-66-1 381209-67-2
381209-68-3 381209-70-7
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(hepatitis C protease NS3 exosite for inhibitor design)

IT 204765-53-7 381209-71-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hepatitis C protease NS3 exosite for inhibitor design)

IT 149885-80-3, Proteinase NS3
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hepatitis C protease NS3 exosite for inhibitor design)

IT **319010-06-5** 319010-33-8 381209-69-4
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(hepatitis C protease NS3 exosite for inhibitor design)

IT 91935-83-0 208521-14-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(hepatitis C protease NS3 exosite for inhibitor design)

IT 381209-73-0P 381209-74-1P 381209-75-2P 381209-76-3P 381209-78-5P
381209-79-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(hepatitis C protease NS3 exosite for inhibitor design)

L12 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:661423 HCAPLUS
DN 135:227016
ED Entered STN: 10 Sep 2001
TI Preparation of N-[1-(4,6-methano-1,3,2-benzodioxaborol-2-yl)-3-butenyl]pyrrolo[1,2-a]pyrazine-6-carboxamides as Hepatitis C virus NS3 protease inhibitors
IN Zhang, Xiaojun; Han, Wei
PA Dupont Pharmaceuticals Company, USA
SO PCT Int. Appl., 191 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D487-04
ICS C07D471-04; A61K031-498; A61K031-55; A61P031-12
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 34

FAN.CNT 1

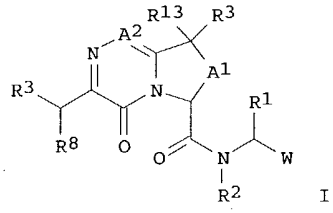
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001064678	A2	20010907	WO 2001-US6269	20010228
WO 2001064678	A3	20020307		

W: AT, AU, BR, CA, CH, CZ, DE, DK, EE, ES, FI, GB, HU, IL, IN, JP, KR, LT, LU, LV, MX, NO, NZ, PL, PT, RO, SE, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

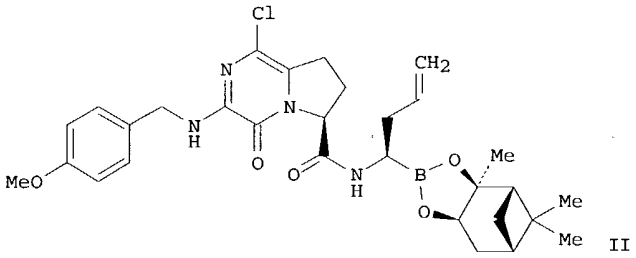
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR
CA 2396504 AA 20010907 CA 2001-2396504 20010228
US 2002065248 A1 20020530 US 2001-795410 20010228
US 6699855 B2 20040302
EP 1261611 A2 20021204 EP 2001-918260 20010228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003525294 T2 20030826 JP 2001-564175 20010228
PRAI US 2000-185618P P 20000229
WO 2001-US6269 W 20010228
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001064678	ICM	C07D487-04
	ICS	C07D471-04; A61K031-498; A61K031-55; A61P031-12
US 2002065248	ECLA	C07F005/02C; C07F005/04

OS MARPAT 135:227016
GI



I



II

AB The present invention relates to the preparation and use of the title compds. (I) [wherein A1 = methylene, ethylene, or propylene; A2 = N or CR6; A3 = amino acid or di- or tripeptide residue, SOR9, SO2R9, COR9, CO2R9, CONHR9, etc.; R9 = H or (un)substituted (cyclo)alkyl, aryl, or heterocyclyl; W = BO2H2, COCOQ, COCONHQ, COCOOQ, COCF2CONHQ, COCF3, COCF2CF3, CHO, amino acid residue, or di- or tripeptide residue; Q = (un)substituted alkyl, alkenyl, alkynyl, amino acid residue, di- or tripeptide residue, etc.; R1 = H, F, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, or aryl; R2 and R8 = independently H, (cyclo)alkyl, alkenyl, or alkynyl; R3 = R4, OR4, SR4, or (un)substituted amino; R4 = (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, or heterocyclyl; R13 = H or alkyl; stereoisomeric forms, stereoisomeric mixts., or pharmaceutically acceptable salt forms thereof] as inhibitors of Hepatitis C virus (HCV) NS3 protease. For example, esterification of Boc-Glu-OMe with EtSH, followed by reduction to the aldehyde using SiEt3H and cyclization in MeOH, gave the 5-methoxy-2-pyrrolidinecarboxylate intermediate. Conversion to the 5-cyano pyroglutamate, deprotection, and cycloaddn. with oxalyl chloride afforded the pyrrolo[1,2-a]pyrazine-6-oxoacetate. Addition of 4-methoxybenzylamine, followed by treatment with LiOH and amidation with Alg-boro-C10H16O2, gave II. A number of compds. I inhibited HCV NS3 protease with Ki values of ≤ 60 μM. The invention also relates to pharmaceutical compns. and diagnostic kits comprising I, and methods of using I for treating viral infection or as an assay standard or reagent.

ST methanobenzodioxaborolylbutenyl pyrrolopyrazinecarboxamide prepn hepatitis C virus protease inhibitor; pyrrolopyrazinecarboxamide methanobenzodioxaborolylbutenyl prepn virucide

IT Hepatitis
(C, infection treatment; preparation of methanobenzodioxaborolylbutenyl

pyrrolopyrazinecarboxamides as HCV NS3 protease inhibitors)

IT Antiviral agents
(preparation of methanobenzodioxaborolylbutenyl pyrrolopyrazinecarboxamides as HCV NS3 protease inhibitors)

IT 149885-80-3, NS3 protease
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Hepatitis C virus; preparation of methanobenzodioxaborolylbutenyl pyrrolopyrazinecarboxamide HCV NS3 protease inhibitors by cyclization of glutamates to pyrrolidines, cycloaddn. with oxalyl chloride, and amidation with boroles)

IT 50715-50-9P 58872-03-0P 99429-45-5P 106665-76-3P 144978-12-1P
158512-77-7P 195964-54-6P 274918-51-3P 284024-88-0P
319010-06-5P 319011-72-8P 319011-74-0P 319011-76-2P
359028-81-2P 359028-82-3P 359028-83-4P 359028-84-5P 359028-85-6P
359028-86-7P 359028-87-8P 359028-89-0P 359028-90-3P 359028-91-4P
359028-92-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of methanobenzodioxaborolylbutenyl pyrrolopyrazinecarboxamide HCV NS3 protease inhibitors by cyclization of glutamates to pyrrolidines, cycloaddn. with oxalyl chloride, and amidation with boroles)

IT 359028-21-0P 359028-22-1P 359028-23-2P 359028-24-3P 359028-25-4P
359028-26-5P 359028-27-6P 359028-28-7P 359028-29-8P 359028-30-1P
359028-31-2P 359028-32-3P 359028-33-4P 359028-34-5P 359028-35-6P
359028-36-7P 359028-37-8P 359028-38-9P 359028-39-0P 359028-40-3P
359028-41-4P 359028-42-5P 359028-43-6P 359028-44-7P 359028-45-8P
359028-46-9P 359028-47-0P 359028-48-1P 359028-49-2P 359028-50-5P
359028-51-6P 359028-52-7P 359028-53-8P 359028-54-9P 359028-55-0P
359028-56-1P 359028-57-2P 359028-58-3P 359028-59-4P 359028-60-7P
359028-61-8P 359028-62-9P 359028-63-0P 359028-64-1P 359028-65-2P
359028-66-3P 359028-67-4P 359028-68-5P 359028-69-6P 359028-70-9P
359028-71-0P 359028-72-1P 359028-73-2P 359028-74-3P 359028-75-4P
359028-76-5P 359028-77-6P 359028-78-7P 359028-79-8P 359028-80-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of methanobenzodioxaborolylbutenyl pyrrolopyrazinecarboxamide HCV NS3 protease inhibitors by cyclization of glutamates to pyrrolidines, cycloaddn. with oxalyl chloride, and amidation with boroles)

IT **319010-09-8P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protease inhibitor; preparation of methanobenzodioxaborolylbutenyl pyrrolopyrazinecarboxamide HCV NS3 protease inhibitors by cyclization of glutamates to pyrrolidines, cycloaddn. with oxalyl chloride, and amidation with boroles)

IT 98-80-6, Phenylboronic acid 1676-90-0 2393-23-9, p-Methoxybenzylamine 2740-83-2, m-(Trifluoromethyl)benzylamine 3886-08-6 4392-24-9, Cinnamyl bromide 6066-82-6, N-Hydroxysuccinimide 7149-65-7, (S)-Ethyl pyroglutamate 13734-41-3 41324-66-7 72086-72-7 323197-73-5 359028-93-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of methanobenzodioxaborolylbutenyl pyrrolopyrazinecarboxamide HCV NS3 protease inhibitors by cyclization of glutamates to pyrrolidines, cycloaddn. with oxalyl chloride, and amidation with boroles)

L12 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:416971 HCAPLUS
DN 135:19916
ED Entered STN: 08 Jun 2001
TI Preparation of α-keto amide inhibitors of hepatitis C virus NS3 protease
IN Han, Wei
PA Du Pont Pharmaceuticals Company, USA
SO PCT Int. Appl., 282 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K005-02
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 15
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001040262	A1	20010607	WO 2000-US32677	20001201
	W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	CA 2390349	AA	20010607	CA 2000-2390349	20001201
	US 2002123468	A1	20020905	US 2000-728653	20001201
	US 6774212	B2	20040810		
	EP 1252178	A1	20021030	EP 2000-983845	20001201
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
	JP 2003526634	T2	20030909	JP 2001-541017	20001201
PRAI	US 1999-168998P	P	19991203		
	WO 2000-US32677	W	20001201		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001040262	ICM	C07K005-02
US 2002123468	ECLA	C07K005/02A; C07K007/02

OS MARPAT 135:19916

AB Keto amide and keto ester compds. R9-A6-A5-A4-A3-A2-NHCR1R2COCO-W-Q [W = NH or O; Q = substituted alkyl, alkenyl, or alkynyl or an amino acid residue; A2 is a bond, NHCH2CO which may be C-substituted, an amino acid residue, or NRCHRCO, where NRCHR represents tetrahydropyrrole-1,2-diyl which may be substituted at the 4- and 5-positions or hexahydroindole-1,2-diyl; A3 or A4 is a bond, NHCH2CO which may be C-substituted, or an amino acid residue; A5 or A6 is a bond or an amino acid residue; R1 = H, F, or substituted alkyl, alkenyl, alkynyl, aryl, or cycloalkyl; R2 = H, F, alkyl; R9 = S(O)R9a, SO2R9a, C(O)R9a, C(O)OR9a, C(O)NHR9a, alkyl-R9a, alkenyl-R9a, or alkynyl-R9a, where R9a = substituted alkyl, cycloalkyl, aryl, or heterocyclyl] or stereoisomeric forms or pharmaceutically acceptable salts were prepared as inhibitors of HCV NS3 protease. Thus, N-(2-pyrazinylcarbonyl)-L-leucyl-L-isoleucyl-3-cyclohexyl-L-alanyl-2-oxo-(3S)-3-aminopentanoylglycine was prepared by a multistep sequence which includes peptide coupling reactions in solution Compds. of the invention exhibit ki values of ≤60 μM, thereby confirming their utility as effective NS3 protease inhibitors.

ST peptide keto amide ester prepn inhibitor NS3 protease; hepatitis C virus protease inhibitor peptide keto amide

IT Hepatitis C virus
(preparation of α-keto amide inhibitors of hepatitis C virus NS3 protease)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of α-keto amide inhibitors of hepatitis C virus NS3 protease)

IT 342612-00-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of α-keto amide inhibitors of hepatitis C virus NS3 protease)

IT **319010-09-8P** 342611-10-3P 342611-11-4P 342611-12-5P
342611-13-6P 342611-15-8P 342611-16-9P 342611-17-0P 342611-18-1P
342611-19-2P 342611-20-5P 342611-21-6P 342611-22-7P 342611-23-8P
342611-24-9P 342611-25-0P 342611-26-1P 342611-27-2P 342611-28-3P
342611-29-4P 342611-30-7P 342611-31-8P 342611-32-9P 342611-33-0P
342611-34-1P 342611-35-2P 342611-36-3P 342611-37-4P 342611-38-5P
342611-39-6P 342611-40-9P 342611-41-0P 342611-42-1P 342611-43-2P
342611-44-3P 342611-45-4P 342611-46-5P 342611-47-6P 342611-48-7P
342611-49-8P 342611-50-1P 342611-51-2P 342611-52-3P 342611-53-4P
342611-54-5P 342611-55-6P 342611-56-7P 342611-57-8P 342611-58-9P
342611-59-0P 342611-60-3P 342611-61-4P 342611-62-5P 342611-63-6P
342611-64-7P 342611-65-8P 342611-66-9P 342611-67-0P 342611-68-1P
342611-69-2P 342611-70-5P 342611-71-6P 342611-72-7P 342611-73-8P
342611-74-9P 342611-75-0P 342611-76-1P 342611-77-2P 342611-78-3P
342611-79-4P 342611-80-7P 342611-81-8P 342611-82-9P 342611-83-0P
342611-84-1P 342611-85-2P 342611-86-3P 342611-87-4P 342611-88-5P
342611-89-6P 342611-90-9P 342611-91-0P 342611-92-1P 342611-93-2P
342611-94-3P 342611-95-4P 342611-96-5P 342611-97-6P 342611-98-7P
342611-99-8P 342612-01-5P 342612-02-6P 342612-03-7P 342612-04-8P

342612-05-9P 342612-06-0P 342612-07-1P 342612-08-2P 342612-09-3P
342612-10-6P 342612-11-7P 342612-12-8P 342612-13-9P 342612-14-0P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of α-keto amide inhibitors of hepatitis C virus NS3 protease)

IT 149885-80-3
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of α-keto amide inhibitors of hepatitis C virus NS3 protease)

IT 59-66-5 61-90-5, L-Leucine, reactions 97-09-6 98-10-2, Benzenesulfonamide 98-64-6 98-97-5, 2-Pyrazinecarboxylic acid 402-46-0 421-85-2, Trifluoromethanesulfonamide 452-35-7 779-71-5 830-43-3 1205-30-7 1431-39-6 1524-40-9 1576-47-2, 2-Naphthalenesulfonamide 1954-92-3 2070-48-6 2295-56-9 3118-68-1 3119-02-6 3144-09-0, Methanesulfonamide 4336-70-3 4371-23-7, 4-Biphenylsulfonamide 4563-33-1, Benzenemethanesulfonamide 4793-24-2 5455-59-4 6325-93-5 6456-74-2 6949-23-1 6961-82-6 7720-45-8 13881-91-9, Aminomethanesulfonic acid 17260-71-8 19797-32-1 21506-01-4 23815-28-3 27527-05-5 29092-27-1 30058-40-3 31602-63-8, 5-(Aminomethyl)tetrazole 35337-99-6 39213-22-4 42918-86-5 51896-27-6 68252-72-2 88568-95-0 91569-33-4, [1,1'-Biphenyl]-3-sulfonamide 148992-43-2 190659-74-6 219138-72-4 253679-11-7 284680-64-4 300382-95-0 323197-73-5 342612-76-4 342612-77-5 342612-78-6 342612-79-7 342612-80-0 342612-81-1 342612-87-7 342612-88-8 342612-89-9 342612-90-2 342612-91-3 342612-92-4 342612-93-5 342612-94-6 342612-95-7 342612-96-8 342612-97-9 342612-98-0 342612-99-1 342613-02-9 342621-41-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of α-keto amide inhibitors of hepatitis C virus NS3 protease)

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of α-keto amide inhibitors of hepatitis C virus NS3 protease)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Akzo Nobel Nv; WO 9850420 A 1998 HCAPLUS
(2) Alkermes Inc; WO 9500535 A 1995 HCAPLUS
(3) Bailey, M; WO 9907734 A 1999 HCAPLUS
(4) Beecham Group Plc; EP 0445467 A 1991 HCAPLUS
(5) Boehringer Ingelheim Ca Ltd; WO 9829435 A 1998 HCAPLUS
(6) Cephalon Inc; WO 9917790 A 1999 HCAPLUS
(7) Deininger, D; WO 9817679 A 1998 HCAPLUS
(8) Georgia Tech Res Inst; WO 9212140 A 1992 HCAPLUS
(9) Zaidan Hojin Biseibutsu; EP 0423358 A 1991 HCAPLUS

L12 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:31525 HCAPLUS
DN 134:101193
ED Entered STN: 12 Jan 2001
TI Preparation of peptide boronic acid inhibitors of hepatitis C virus protease
IN Kettner, Charles A.; Jagannathan, Sharada; Forsyth, Timothy Patrick
PA Du Pont Pharmaceuticals Company, USA
SO PCT Int. Appl., 258 pp.
CODEN: PIXXD2
DT Patent

LA English
IC ICM C07K
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 10, 29, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001002424	A2	20010111	WO 2000-US18655	20000707
	WO 2001002424	A3	20010719		
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	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2376965	AA	20010111	CA 2000-2376965	20000707
	AU 2000057888	A5	20010122	AU 2000-57888	20000707
	EP 1196436	A2	20020417	EP 2000-943413	20000707
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PRAI	US 1999-142561P	P	19990707		
	WO 2000-US18655	W	20000707		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001002424	ICM	C07K

OS MARPAT 134:101193
AB α-Aminoboronic acids and corresponding peptide analogs R3-A-NR2CHR1BY1Y2 [Y1, Y2 = OH, F, an amino group, alkoxy or BY1Y2 is a cyclic boron ester, amide or amide-ester; R1 = CH:CH2, CH2CH:CH2, CH:CHCH3, C.tplbond.CH, C.tplbond.CCH3, CH2C.tplbond.CH, cyclopropyl, cyclopropylmethyl, cyclobutyl, cyclobutylmethyl, mercaptoalkyl, alkyldithioalkyl, etc.; A is a bond, a natural or unnatural amino acid residue, or a peptide residue comprising 2-10 amino acids; R2 = H, alkyl, aryl, arylalkyl, cycloalkyl; R3 = H, alkanoyl, alkyl, alkenyl, alkynyl, aryl, carbalkoxy, alkylsulfinyl, alkylsulfonyl, carbamoyl, etc.] were prepared for the treatment of hepatitis C viral infections. Thus, Boc-Asp(OBu-t)-Glu(OBu-t)-Val-Val-Pro-boroCpa-OH pinanediol ester (Boc = tert-butoxycarbonyl, boroCpa is L-2-amino-3-cyclopropylboronic acid residue) was prepared by standard methods of peptide coupling in solution Enzyme assays, dosages and formulations are discussed.
ST peptide boronic acid prepn inhibitor hepatitis C virus protease
IT Peptides, preparation
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(boronic; preparation of peptide boronic acid inhibitors of hepatitis C virus protease)
IT Hepatitis C virus
(preparation of peptide boronic acid inhibitors of hepatitis C virus protease)
IT 149885-80-3, Hepatitis C virus protease
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of peptide boronic acid inhibitors of hepatitis C virus protease)
IT 96-33-3, Methyl acrylate 98-80-6, Phenylboronic acid 98-97-5, Pyrazinecarboxylic acid 108-98-5, Thiophenol, reactions 359-07-9 460-37-7, 3,3,3-Trifluoropropyl iodide 593-71-5, Chloroiodomethane 931-59-9, Phenylsulfenyl chloride 1730-25-2, Allylmagnesium bromide 2177-63-1 2719-27-9, Cyclohexanecarbonyl chloride 4333-56-6, Cyclopropyl bromide 5292-43-3, tert-Butyl bromoacetate 5419-55-6, Triisopropyl borate 6009-07-0 18680-27-8 54631-81-1 76347-13-2 84110-32-7 85893-32-9 90084-27-8 94242-85-0 252357-27-0 319011-12-6 319011-95-5 319012-18-5 319012-20-9
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(preparation of peptide boronic acid inhibitors of hepatitis C virus protease)
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide boronic acid inhibitors of hepatitis C virus protease)

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RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide boronic acid inhibitors of hepatitis C virus protease)

IT 319006-73-0P 319006-75-2P 319006-77-4P 319006-79-6P 319006-81-0P

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RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide boronic acid inhibitors of hepatitis C virus protease)

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AN 2004-613830 [59] WPIX
CR 2003-465950 [44]
DNC C2004-221320
TI New peptide compounds are hepatitis C virus NS3 protease inhibitors used in treatment of e.g. hepatitis C viral infections.
DC B04 B05
IN PRIESTLEY, E S
PA (PRIE-I) PRIESTLEY E S
CYC 1

PI US 2004147483 A1 20040729 (200459)* 54 A61K031-69 <--
ADT US 2004147483 A1 Div ex US 2001-39317 20011023, US 2004-759725 20040115
PRAI US 2001-39317 20011023; US 2004-759725 20040115
IC ICM A61K031-69
ICS A61K031-195
AB US2004147483 A UPAB: 20040915
NOVELTY - Peptide compounds (I), are new.
DETAILED DESCRIPTION - Peptide compounds of formula R3-A-N(R2)-CH(R1)-W (I), their stereoisomers, salts and prodrugs are new.
W = B'(Y1)(Y2), C(O)C(O)-Q, C(O)C(O)NH-Q, C(O)C(O)-O-Q, C(O)CF2C(O)NH-Q, C(O)CF3, C(O)CF2CF3 or C(O)H;
Y1, Y2 = OH, F, NR4R5 or 1-8C alkoxy, or
B'Y1Y2 = 2-20C cyclic boronic ester, 20C cyclic boronic amide or 2-20C cyclic boronic amide-ester (all optionally containing 1-3 N, S or O heteroatoms);
Q = 2-4C alkenyl or 2-4C alkynyl (both substituted by Q1), (CR6R6c)p-Q1, (CR6R6c)p-Q2 or amino acid residue;
p = 1-4;
Q1 = aryl or 5- or 6-membered heterocyclyl containing 1-4 O, S or N heteroatoms (both optionally substituted by 1-4 Q1a), CO2R7, SO2R7, SO3R7, P(O)2R7 or P(O)3R7;
Q1a = H, F, Cl, Br, I, NO2, CN, NCS, CF3, OCF3, CO2R8, C(O)NR8R9, NHC(O)R8, SO2R8, SO2NR8R9, NR8R9, OR8, SR8, 1-4C alkyl, 1-4C haloalkyl or 1-4C haloalkoxy;
Q2 = X1-NR10-Z, NR10-X2-Z or X1-NR10-X2-Z;
X1, X2 = CO, S, SO, SO2, P(O), P(O)2 or P(O)3;
Z = 1-4C alkyl, 2-4C alkenyl or 2-4C alkynyl (all optionally substituted by 1-3 Za), 3-10C cycloalkyl, 3-10C carbocyclyl or 6-10 membered aryl (all optionally substituted by 1-5 Zb), 1-4C haloalkyl or 5-10 membered heterocyclyl containing 1-4 O, S or N heteroatoms (optionally substituted by 1-4 Zb);
Za = 3-7C cycloalkyl, 3-10C carbocylyl or 6-10 membered aryl (all optionally substituted by 1-5 Zb), H, F, Cl, Br, I, NO2, CN, NCS, CF3, OCF3, CO2R8, C(O)NR8R9, NHC(O)R8, NR8R9, OR8, SR8, S(O)R8, SO2R8, SO2NR8R9, 1-4C alkyl, 1-4C haloalkyl, 1-4C haloalkoxy or 5-10 membered heterocyclyl containing 1-4 O, S or N heteroatoms optionally substituted by 1-4 Zb);
Zb = 3-7C cycloalkyl, 3-10C carbocylyl or 6-10 membered aryl (all optionally substituted by 1-5 Zc), H, F, Cl, Br, I, NO2, CN, NCS, CF3, OCF3, CO2R8, C(O)NR8R9, NHC(O)R8, NR8R9, OR8, SR8, S(O)R8, SO2R8, SO2NR8R9, 1-4C alkyl, 1-4C haloalkyl, 1-4C haloalkoxy or 5-10 membered heterocyclyl containing 1-4 O, S or N heteroatoms (optionally substituted by 1-4 Zc);
Zc = H, F, Cl, Br, I, NO2, CN, CS, CF3, OCF3, CO2R8, C(O)NR8R9, NHC(O)R8, NR8R9, OR8, SR8, S(O)R8, SO2R8, SO2NR8R9, 1-4C alkyl, 1-4C haloalkyl or 1-4C haloalkoxy;
A = A2-A3, A2-A3-A4, A2-A3-A4-A5, A2-A3-A4-A5-A6 or A2-A3-A4-A5-A6-A7;
A2 = natural, modified or unnatural amino acid in D or L configuration, or a group of formula (i);
Rx = H, F, Cl, Br, I, CF3, OCF3, (CH2)m-R16-(CH2)n-R12 or CO2R12;
m, n = 0-3;
A3-A7 = natural, modified or unnatural amino acid in D or L configuration;
R1 = CH2CH2-R1a, CH2CH2CH2-R1a, CH2CH2CH2CH2-R1a, CH2CH2CH2CH2CH2-R1a, CH2CH2CH2CH2CH2CH2-R1a, CH2CH2CH2CH2CH3, CH2CH2CH2CH2CH2CH3, CH2CH2CH2C(CH3)2, CH2CH2CH2C(CH2CH3)2 or CH2CH2CH2-cyclobutyl;
R1a = a group of formula (ii);
R1b = H, 1-4C alkyl, F, Cl, Br, I, OH, 1-4C alkoxy, phenoxy, benzyloxy, SH, CN, NO2, C(O)OR1d, NR1dR1d, CF3, OCF3, 3-6C cycloalkyl or aryl (optionally substituted by 1-3 R1c);
R1c = CH3, ethyl, Cl, F, Br, I, OH, methoxy, ethoxy, CN, NO2, C(O)OR1d, NR1dR1d, CF3 or OCF3;
R1d = H, 1-4C alkyl, phenyl or benzyl;
R2 = H, 1-4C alkyl, aryl, aryl-1-4C alkyl or 3-6C cycloalkyl;
R3 = H, 1-4C alkyl, aryl, aryl-1-4C alkyl, C(O)R11, CO2R11, C(O)NHR11, SOR11, SO2R11 or NH2 blocking group;
R4, R5 = H, 1-4C alkyl, aryl-1-4C alkyl or 3-7C cycloalkyl;
R6 = H, CO2R7, NR7R7 or 1-6C alkyl (optionally substituted by R6a);
R6a = halo, NO2, CN, CF3, CO2R7, NR7R7, OR7, SR7, C(=NH)NH2 or aryl (optionally substituted by R6b);
R6b = CO2H, NH2, OH, SH or (=NH)NH2;
R6c = H or 1-4C alkyl;
R7 = aryl or aryl-1-4C alkyl (both aryl substituted by 1-3 CH3, NO2, CN, OH, OCH3, SO2CH3, CF3, Cl, Br, I or F), H or 1-4C alkyl, or

NR7R7 = 5- or 6-membered heterocyclyl containing a N atom and optionally a second O, S or N heteroatom;
R8, R9 = H, 1-4C alkyl, aryl, aryl-1-4C alkyl or 3-7C cycloalkyl, or
NR8R9 = 5- or 6-membered heterocyclyl containing a N atom and optionally a second O, S or N heteroatom;
R10 = 1-4C alkyl, 3-10C carbocyclyl, 6-10 membered aryl or 5-10 membered heterocyclyl containing 1-4 O, S or N heteroatoms (all optionally substituted by 1-3 R13) or H;
R11 = 1-4C alkyl (optionally substituted by R11a), or 6-10 membered aryl or 5-10 membered heterocyclyl containing 1-4 O, S or N heteroatoms (both optionally substituted by 1 or 2 R11b);
R11a = 1-4C alkyl, halo, OR14, SR14, NR14R15, aryl or 5- or 6-membered heterocyclyl containing 1-3 N, O or S heteroatoms;
R11b = aryl or aryl-1-4C alkyl (both optionally aryl substituted by 1-3 CH3, NO2, CN, OH, OCH3, SO2CH3, CF3, Cl, Br, I or F), NO2, NH2, SO3H, SO2CH3, CO2H, CF3, OH, SH, OCF3, Cl, Br, I, F, O, 1-4C alkyl, 1-4C alkoxy or 1-4C thioalkoxy;
R12 = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-7C cycloalkyl, 4-10C (cycloalkylalkyl) or 6-10 membered aryl (all optionally substituted by 1-3 R12a), H or 5-10 membered heterocyclyl containing 1-4 O, S or N heteroatoms (optionally substituted by 1 or 2 R12a);
R12a = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-7C cycloalkyl, 4-10C (alkylcycloalkyl) or 6-10 membered aryl (all optionally substituted by 1-3 R12b), 1-6C alkoxy, lower thioalkyl, sulfonyl, NO2, halo, haloalkyl, carboxyl, carboxy(lower alkyl), OR14, SR14, NR14R15, C(=O)NR14R15, NR14C(O)R15, SO2R14 or 5-10 membered heterocyclyl containing 1-4 O, S or N heteroatoms (optionally substituted by 1 or 2 R12b);
R12b = 1-6C alkyl, 3-7C cycloalkyl, 1-6C alkoxy, halo, OR14, SR14, NR14R15, C(O)NR14R15, NR14C(O)R15, SO2R14, NO2, haloalkyl, carboxyl, carboxy(lower alkyl), aryl or 5-10 membered heterocyclyl containing 1-4 O, S or N heteroatoms (optionally substituted by 1-6C alkyl);
R13 = H, NO2, SO2OH, SO2CH3, CF3, Cl, Br, I, F, NH2, NH(CH3), N(CH3)2, NH(CH2CH3), N(CH2CH3)2 or 1-4C alkyl;
R14, R15 = H, 1-4C alkyl, aryl, aryl(1-4C alkyl) or 3-7C cycloalkyl;
R16 = a bond, O, S or NR17, and
R17 = H, 1-4C alkyl, aryl, aryl(1-4C alkyl) or 3-6C cycloalkyl.
ACTIVITY - Virucide; Antiinflammatory; Hepatotropic.
MECHANISM OF ACTION - Hepatitis C virus NS3 protease inhibitor.
In an in vitro assay, results showed that (I) exhibited Ki values of upto 50 mu M for inhibiting NS3 protease.
USE - Used for treating viral infections (particularly hepatitis C viral infections) (claimed).
Dwg.0/0

FS CPI
FA AB; GI; DCN
MC CPI: B04-C01A; B05-B01A; B05-B01E; B05-B01F; B05-B01G; B05-B01J; B05-B01K; B05-B01L; B05-B01M; B05-B01N; B05-B01P; B06-H; B07-H; B10-A09B; B10-A10; B10-A15; B10-C04; B10-D03; B14-A02; B14-C03; B14-D03; B14-N12

L18 ANSWER 2 OF 2 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2003-465950 [44] WPIX
CR 2004-613830 [59]
DNC C2003-124173
TI New class of peptides are inhibitors of hepatitis C virus NS3 protein, useful for treating e.g. hepatitis.
DC B05
IN PRIESTLEY, E S
PA (PRIE-I) PRIESTLEY E S
CYC 1
PI US 2002177725 A1 20021128 (200344)* 54 C07F005-02 <--
ADT US 2002177725 A1 **Provisional US 2000-242557P 20001023**, US 2001-39317 20011028
PRAI **US 2000-242557P 20001023**; US 2001-39317 20011028
IC ICM C07F005-02
ICS C07C237-04; C07F005-05
AB US2002177725 A UPAB: 20040915
NOVELTY - Peptides (I) are new.
DETAILED DESCRIPTION - Peptides of formula R3-A-N(R2)-CH(R1)-W (I), their stereoisomers, salts or prodrugs are new.
W = e.g. -C(=O)CF3, -C(=O)CF2CF3 or -C(=O)H;
A = e.g. A2-A3;
A2 = e.g. natural amino acid or a modified amino acid;
A3, A4 = an amino acid residue selected from a natural amino acid, a modified amino acid or an unnatural amino acid;

R1 = e.g. -(CH2)4CH3, -(CH2)5CH3 or -(CH2)3C(CH3)2;
R2, R3 = e.g. H, 1-4C alkyl or aryl.
Full definitions are given in the Definitions (Full Definitions) Section.
ACTIVITY - Hepatotropic; Virucide; Antiinflammatory.
MECHANISM OF ACTION - Serine Protease Inhibitor; Hepatitis C Virus (HCV) NS3 Protease Inhibitor.
In an assay to determine inhibitory selectivity of HCVNS3 protease over elastase, H-Asp-Glu-Val-Val-Pro-(1R)-1-amino-3-phenylpropylboronic acid (+)-pinanediol ester (Ia) displayed a 10-fold selectivity for HCVNS3 over elastase.
USE - For treating viral infections e.g. Hepatitis C virus (HCV) infections (claimed).
ADVANTAGE - The compounds have HCV NS3 protease inhibitory selectivity over inhibition of elastase and chymotrypsin.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-C01A; B07-D03; B14-A02A7

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